MAY 2 2 2014

510(k) Summary

This summary of 510(k) substantial equivalence information is being submitted in accordance with the requirements of 21 CFR 807.92.

Assigned 510(k) number:	K140426
Submitted by:	Centers for Disease Control and Prevention 1600 Clifton Road NE Atlanta, GA 30333
Contact Person:	CDR Yon Yu, Pharm.D. Associate Director for Regulatory Affairs Office of the Director National Center for Emerging and Zoonotic Infectious Diseases Centers for Disease Control and Prevention (Registration number: 1050190) 1600 Clifton Road, NE, MS C-18 Atlanta, GA 30333 (404) 639-3046 (office) (404) 639-1275 (fax) Fkb8@cdc.gov
Date prepared:	February 14, 2014
Device trade name:	*B. anthracis* Real-time PCR Assay
Classification name and regulation:	*In vitro* diagnostic device for *Bacillus spp.* detection; 21 CFR 866.3045
Product Code:	NHT
Class:	II
Panel:	Microbiology (83)
Predicate device(s):	JBAIDS Anthrax Detection System (K051713, K071188) November 18, 2005

Background

Anthrax is a zoonotic disease caused by *B. anthracis* that is transmissible to humans through handling or consumption of contaminated animal products. Infection can also occur through inhalation of *B. anthracis* spores from contaminated animal products such as wool or hides. Infection caused by human-to-human contact has been reported only rarely, and only via the cutaneous route (Versalovic, 2011). There have been 3 major presentations of anthrax in humans: cutaneous, ingestion, and inhalation. In cases of

cutaneous anthrax, patients typically present with a painless blister or skin ulcer with a black area in the center. Inhalation anthrax is typically associated with cold or flu-like symptoms, cough, chest discomfort, shortness of breath, fatigue, and muscle aches. Symptoms of gastrointestinal anthrax typically include nausea, loss of appetite, bloody diarrhea, fever and severe stomach pain.

Prior to the development of the LRN *B. anthracis* Real-time PCR Assay, identification of *B. anthracis* was determined by using phenotypic differences between *B. anthracis* and the rest of the *B. cereus* group. (i.e. lack of motility and hemolysis, susceptibility to penicillin, colony morphology, susceptibility to lysis by gamma phage) (Hoffmaster, 2002). However, these methods require growth of the microorganism and can take at least 24 hours incubation to obtain a result. Due to the prevalence of *B. anthracis* in the environment, and its past use as a biological weapon, it has long been an organism of concern. The use of *B. anthracis* in the bioterrorism attacks of 2001 resulting in cases of inhalation and cutaneous anthrax increased public health concern and reinforced the worry that it would be used in the same way again. For these reasons, there was a need for rapid testing to aid in the identification of *B. anthracis*. The Laboratory Response Network (LRN) is part of a national bioterrorism preparedness initiative and one of the major goals of this initiative is the development and validation of rapid and specific assays for agents likely to be used in a bioterrorism event. Accordingly, scientists at the Centers for Disease Control and Prevention have developed several real-time PCR based assays to detect *B. anthracis* and other potential agents of bioterrorism in an effort to meet the need for rapid detection.

Device description

The *B. anthracis* Real-time PCR Assay uses a fluorogenic probe, consisting of an oligonucleotide with a reporter dye (FAM) attached to the 5′ end and a quencher dye (BHQ1) attached at or near the 3′ end. The probe anneals to a specific target sequence located between the forward and reverse primers. During the extension phase of the PCR cycle, the 5′ nuclease activity of Taq polymerase degrades the probe causing the reporter dye to separate from the quencher dye and a fluorescent signal is generated. With each cycle, additional reporter dye molecules are cleaved from their respective probes and the fluorescence intensity is monitored during the PCR. The Taq polymerase used in this assay is inactive at room temperature. It must be activated by incubation at 95°C, which also minimizes the production of nonspecific amplification products.

Each extracted DNA sample is tested with three *B. anthracis* primer and probe sets run as individual reactions. The primer and probe sets target genes encoding virulence factors as well as conserved regions of DNA from the *B. anthracis* chromosome. All three primer and probe sets must be positive for the overall result of the *B. anthracis* Real-time PCR Assay to be interpreted as positive. Any result that is positive for some, but not all three target regions,

is still considered equivocal and follow-up laboratory investigation should be performed per the LRN *Bacillus anthracis Testing Algorithm*.

Intended Use

The *B. anthracis* Real-time PCR Assay is an *in vitro* diagnostic test for the qualitative detection of plasmid and chromosomal DNA sequences from *B. anthracis*. The assay can be used to test human respiratory samples, whole blood, serum, plasma, swabs from lesions, CSF, pleural fluid, and bacterial culture isolates from individuals suspected of having anthrax.

Results generated from direct specimen testing are presumptive for the identification of *B. anthracis*. Results generated from culture isolate testing should be used in conjunction with other conventional methods for identification of *Bacillus anthracis* isolates as part of the LRN *Bacillus anthracis Testing Algorithm*. The diagnosis of anthrax infection must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidences in addition to the identification of *B. anthracis* from cultures or detection directly in clinical specimens.

Use is limited to Laboratory Response Network (LRN) designated laboratories.

The *B. anthracis* Real-time PCR Assay is also intended for environmental specimen testing for biothreat detection and response. FDA has not evaluated claims related to the use of this assay on environmental specimens.

Device comparison

As previously mentioned, there are several culture based methods used for identification of B. *anthracis*. While they are reliable methods, they do not offer a fast result since a pure culture of the microorganism must first be isolated, then set up with each test (gamma phage, morphology, motility, penicillin resistance, etc.). Each of these tests requires approximately 24 hours incubation before they can be interpreted. There is a currently marketed device that uses similar nucleic acid amplification and fluorescent probe detection technology called the JBAIDS Anthrax Detection System (Idaho Technology, Inc., 510(k) #K051713). The following table summarizes the similarities and differences between the two devices.

Device (Owner)	*B. anthracis* Real-time PCR Assay (Centers for Disease Control and Prevention)	JBAIDS Anthrax Detection System (Idaho Technology, Inc.)
	Similarities	
Intended Use	The *B. anthracis* Real-time PCR Assay is an *in vitro* diagnostic test for the qualitative detection of plasmid and chromosomal DNA sequences from *B. anthracis.* The assay can be used to test human respiratory samples, whole blood, serum, plasma, swabs from lesions, CSF, pleural fluid, and bacterial culture isolates from individuals suspected of having anthrax. Results generated from direct specimen testing are presumptive for the identification of *B. anthracis.* Results generated from culture isolate testing should be used in conjunction with other conventional methods for identification of *Bacillus anthracis* isolates as part of the LRN *Bacillus anthracis Testing Algorithm*. The diagnosis of anthrax infection must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidences in addition to the identification of *B. anthracis* from cultures or detection directly in clinical specimens. **Use is limited to Laboratory Response Network (LRN) designated laboratories.** The *B. anthracis* Real-time PCR Assay is also intended for environmental specimen testing for biothreat detection and response. FDA has not evaluated claims related to the use of this assay on environmental specimens.	The JBAIDS Anthrax Detection System is a real-time polymerase chain reaction (PCR) test system intended for the qualitative *in vitro* diagnostic (IVD) detection of target DNA sequences on the pXO1 plasmid (Target 1) and the pXO2 plasmid (Target 2) from *Bacillus anthracis.* The system can be used to test human whole blood collected in sodium citrate from individuals suspected of having anthrax, positive blood cultures, and cultured organisms grown on blood agar plates. The JBAIDS Anthrax Target 2 assay is used as a supplementary test only after a positive result with the Target 1 Assay. The JBAIDS Anthrax Target 1 and Target 2 Assays are run on the JBAIDS instrument using the Diagnostic Wizard. Results are for the presumptive identification of *B. anthracis,* in conjunction with culture and other laboratory tests. The following considerations also apply: • The diagnosis of anthrax infection must be made based on history, signs, symptoms, exposure likelihood, other laboratory evidence, in addition to the identification of pXO1 and pXO2 targets either from cultures or from direct blood specimens. • The assays have not been evaluated with blood from individuals without clinical signs or symptoms who

		were presumed exposed and who subsequently developed anthrax (inhalation or other forms of the disease), or from individuals with any form of anthrax (inhalational, cutaneous, or gastrointestinal). • The level of plasmid targets that would be present in blood from individuals with early systemic infection is unknown. • The definitive identification of *B. anthracis* from colony growth, liquid blood culture growth, or from blood specimens requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reports are required. The safety and effectiveness of other types of tests or sample types (not identified as "For *in vitro* diagnostic use") have not been established.
Principle of Operation	Nucleic acid amplification and fluorescent probe detection	Nucleic acid amplification and fluorescent probe detection

Differences		
Sample Types	• Swabs from lesions and vesicular material • Whole blood (EDTA or sodium citrate) • Serum/Plasma • Respiratory specimens (transtracheal aspirates, bronchial lavage, and sputum) • Cerebrospinal fluid • Pleural fluid • Bacterial culture isolates • Environmental samples collected for investigational or surveillance use	Whole blood (sodium citrate)
Instrumentation	Applied Biosystems 7500 Fast Dx Real-Time PCR System and Cepheid SmartCycler I or II Instruments with native software	JBAIDS integrated thermocycler and fluorimeter with Diagnostic Wizard software
Targets	*B. anthracis* virulence plasmids and chromosomal region DNA	*B. anthracis* virulence plasmids

Establishment of Performance Characteristics

Inquiries regarding performance characteristics for the *B. anthracis* Real-time PCR Assay should be directed to the Centers for Disease Control and Prevention.

Limit of Detection (LoD)

The limit of detection for the *B. anthracis* Real-time PCR Assay was determined through in-house and multicenter sensitivity studies.

Analytical Sensitivity and Specificity

Inquiries regarding performance characteristics for the *B. anthracis* Real-time PCR Assay should be directed to the Centers for Disease Control and Prevention.

Clinical Performance

Clinical performance of the *B. anthracis* Real-time PCR Assay was established through three evaluations: a) Evaluation of the BA3 marker to identify *B. anthracis* in a historical collection of *Bacillus sp.* isolates; b) Testing of known *B. cereus* isolates using the *B. anthracis* Real-time PCR Assay; c) Testing of known bacterial isolates using the *B. anthracis* Real-time PCR Assay. All three data sets compared the performance of the *B. anthracis* Real-time PCR Assay to a battery of tests performed by the CDC, including the gamma phage lysis, conventional culture, microbiological, and biochemical testing.

Repeatability in clinical matrices was determined through a multicenter study.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

May 22, 2014

CENTERS FOR DISEASE CONTROL AND PREVENTION
YON YU
ASSOCIATE DIRECTOR FOR REGULATORY AFFAIRS
LABORATORY PREPAREDNESS AND RESPONSE BRANCH
NCEZID/DPEI
1600 CLIFTON RD. NE, MS C-18
ATLANTA, GA 30333
USA

Re: K140426
Trade/Device Name: *B. anthracis* Real-Time PCR Assay
Regulation Number: 21 CFR 866.3045
Regulation Name: *In vitro* Diagnostic Devices for *Bacillus* spp. Detection
Regulatory Class: II
Product Code: NHT
Dated: February 14, 2014
Received: February 25, 2014

Dear Ms. Yu:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

John Hobson -S for

Sally A. Hojvat, M. Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement on last page.

510(k) Number *(if known)*

K140426

Device Name

B. anthracis Real-Time PCR Assay

Indications for Use *(Describe)*

The *B. anthracis* Real-Time PCR Assay is an *in vitro* diagnostic test for the qualitative detection of plasmid and chromosomal DNA sequences from *B. anthracis*. The assay can be used to test human respiratory samples, whole blood, serum, plasma, swabs from lesions, CSF, pleural fluid, and bacterial culture isolates from individuals suspected of having anthrax.

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Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

John Hobson -S
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